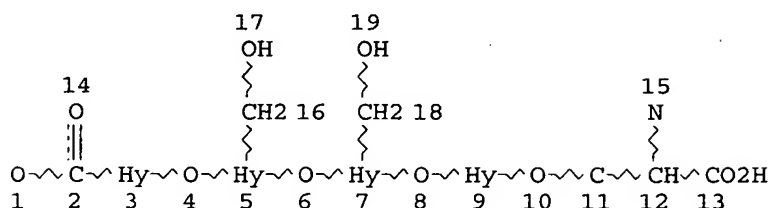


10/808791

GGCAT IS UNS AT 3
GGCAT IS MCY SAT AT 5
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE
L6 STR



NODE ATTRIBUTES:
CONNECT IS X1 RC AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L7 417 SEA FILE=REGISTRY SUB=L2 SSS FUL (L3 OR L4 OR L5 OR L6)
L8 92 SEA FILE=REGISTRY ABB=ON PLU=ON L7 AND NA=>1

One or more
Sodiums present

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L10 10 S L9 NOT (PY=>2002 OR PD=>20020923)

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dated prior to 09-23-02

E1 THROUGH E30 ASSIGNED

L10 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:601171 HCAPLUS

DOCUMENT NUMBER: 131:308098

TITLE: Heparin dodecasaccharide binding to platelet factor-4 and growth-related protein- α . Induction of a partially folded state and implications for heparin-induced thrombocytopenia

AUTHOR(S): Mikhailov, Dmitri; Young, Helen C.; Linhardt, Robert J.; Mayo, Kevin H.

CORPORATE SOURCE: Department of Biochemistry, Molecular Biology & Biophysics, Biomedical Engineering Center, University of Minnesota Health Science Center, Minneapolis, MN, 55455, USA

SOURCE: Journal of Biological Chemistry (1999), 274(36), 25317-25329

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB α -Chemokines are known heparin-binding proteins. Here, a heparin dodecasaccharide (H12) was purified and used in NMR studies to investigate binding to growth-related protein- α (Gro- α) and to platelet factor-4-M2 (PF4-M2), an N-terminal chimera of PF4. Pulsed field gradient NMR was used to derive diffusion coeffs. as the protein (monomer):H12 ratio was varied. In the absence of H12, both PF4-M2 and Gro- α give diffusion coeffs. consistent with the presence of mostly dimers. As the PF4-M2:H12 ratio is increased from 1:6 to 2:1, the diffusion coefficient increases, indicating dissociation to the monomer state. On addition of H12 to either protein, $^{15}\text{N}/^1\text{H}$ heteronuclear single quantum coherence NMR data demonstrate loss of ^1H resonance dispersion and intensity, particularly at protein:H12 ratios of 2:1 to 4:1, indicating significant perturbation to native structures. For Gro- α in particular, ^1H resonance dispersion appears random coil-like. At these same ratios, CD data show general retention of secondary structure elements with a slight shift to addnl. helix formation. Random coil NMR resonance dispersion suggests a shift to a less compact, partially folded, and/or more flexible state. Further addition of H12 causes resonance intensity and dispersion to return making NMR spectra appear native-like. At low PF4-M2:H12 ratios, loss of resonance intensity for residues proximal to Arg-20 and Arg-22 in three-dimensional NMR HCCH-TOCSY spectra suggests that the Arg-20-Arg-22 loop either interacts most strongly with H12 and/or that binding at this site is heterogeneous. This domain was previously shown to be crucial to heparin binding. Of particular interest to the biol. of PF4-heparin complex formation, heparin-induced thrombocytopenia antibody binding occurs at about the same PF4-M2:H12 ratio as does this transition to a partially folded PF4-M2 state, strongly suggesting that heparin-induced thrombocytopenia antibody recognizes a less folded, lower aggregate state of the protein.

IT 164082-56-8

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(structural alterations in heparin dodecasaccharide binding to platelet factor-4 and growth-related protein- α and implications for heparin-induced thrombocytopenia)

RN 164082-56-8 HCAPLUS

CN D-Glucose, O-4-deoxy-2-O-sulfo- α -L-threo-hex-4-enopyranuronosyl-